CHAPTER 4

Discussion

The causes of autoimmune diseases (ADs) are still not clearly known but it is believed that diseases are motivated by multiple factors including genetic, hormone and environment factors. For the environmental factors that trigger ADs, infection (virus, bacteria and other pathogens) is one of the important factors [84]. In the present study, we seek to disclose whether and how HIV infection instigate autoimmune diseases. Therefore, we investigated the prevalence of antinuclear antibodies (ANA) in HIV infected individuals compared to healthy donors. Currently, measurement of ANA is a necessary means used to assist the diagnosis of ADs. Upon detection of ANA in our recruited participants, we found that the prevalence of ANA in HIV-infected individuals was 25% and in healthy donor was 22%. Though, the difference of the prevalence between these two groups was not statistically significant, the tendency of the prevalence seems to be higher in HIV-infected group. The ANA prevalence in HIV-positive persons presented here was higher than that were reported by Kulthanan et al. [85] and Krishnan and colleague [86] which were 3 and 6.8 %, respectively. It is necessary to point out that the majority of individuals in our study were positive at significant titer, though still had low level (1:80) that might not indicate strong support between the association of ANA and ADs. However, this study is crossectional, therefore, following up the ANA level in this group of patients at later times is suggested to expand the evidence. Nevertheless, this level of ANA has also been amounted in HIV infection investigated by others as well as in other infections such as hepatitis B, hepatitis C, HTLV, and syphilis [87-89]. Autoimmune disease-mimicking symptoms like fevers, lymphadenopathy, photosensitivity, rash, renal dysfunction, neurological haematolo-gical disorders and polyarthralgias have been frequently seen in patient with HIV infection [90, 91]. But often time, these symtomps did not attribute to ADs. ANA positive can be found in healthy individual. The prevalence found in the

previous studies vary from 4% to 22.6% [88, 89, 92-95] with mostly in low titer which is in accordance with the result in this study. These findings marked that the diagnosis criteria for ADs do not solely depend on ANA. In adittion, we also found participants with high titer of ANA. There were 6 (22.7%) donors and 7 (36.8%) patients who were positive with ANA titer 160 and above. It might be interesting to follow up these subjects for any sign of autoimmune disease development.

In this study, ANA positive result in female healthy donor tends to be higher than in male which accorded with the previous studies [88, 89, 92-96]. However, in HIV infected patient group, ANA positive result in male seemed to be higher than in female. From the literature, female displayed a higher risk of ANA positive, assuming that estrogen may play an important role [89]. In addition, there was no statistic significant difference of age between ANA positive and negative groups in our study but the highest ANA prevalence was found in the oldest group (51- to 60-year) which accorded the inspection reported in the literature of higher ANA positive result in elderly [89, 92, 93, 97]. In HIV-infected patients there were no statistic significant difference of CD4 cells and infection duration between ANA positive and negative groups. For infection duration, the highest prevalence of ANA positive was found in the highest infection duration group (21- to 25-year), suspecting that chronic infection may play the role in ANA production.

Th17 and Treg cells have an opposite role in the immune system. Whereas Th17 cells stimulate proinflammatory response and can stimulated autoimmunity, T- reg cells control the expansion and function of effector cells including the maintenance of self-tolerance. Therefore, loss of equilibrium between these two cells could lead to autoimmune and inflammatory diseases due to the imbalance of immune response. In HIV infection, abnormalities were found in all major lymphocyte populations due to the chronic immune activation, and autoantibody production in HIV-infected patients have also been suggested [14, 70]. Moreover, there are several reports regarding the association between HIV infection and autoimmune diseases [85, 98-103]. Therefore, the present study was to assess the balance between Th17 and Treg cells in HIV infected patients in different setting of ANA outcomes. The subjects were divided into 4 groups;1) HIV negative with ANA negative, 2) HIV negative with ANA positive, 3) HIV positive with ANA negative, and 4) HIV positive with ANA positive. The result

showed that there was no statistical significant difference of Th17, Treg or Th7/Treg ratio among those 4 groups. It should be emphasized that the MFI of Th17 cells in HIV-infected individuals seem to be higher than in healthy donor which indicated the higher production of IL-17 in these patients, hence, higher inflammatory response. Although the patients have been habouring the HIV on the average of 10 years, we attempted to explain the still balance of Th17/Treg seen in HIV-infected groups compare to that of donor groups might be due to the fact that the patients have been receiving cART and were able to suppress the virus to the point that might not burden the imbalance of the immune cells sufficiently. Several reports suggested that highly active antiretroviral therapy (HAART) affected Th17 and Treg cells in HIV infection [104, 105]. DaFonsece and colleague suggested that Th17 cells were increased and inflammation markers were decreased during HAART [106]. Montes and colleague reported that HAART therapy can normalize Treg cells level in HIV infected patient to the similar level of healthy controls [107]. Rueda et al., Anderson et al., as well as Mendezz-Lagares and their colleague mentioned that patients who did not respond to HARRT had higher Treg cells numbers than responders [108-110]. Furthermore, many studies reported the impact of viral load on Th17 and Treg cells. Ndhlovu and colleague suggested that HIV-infected children had a lower frequency of Th17 cells than healthy children and infected children with undetectable viral load had a higher Th17 cell level than infected children with >50 copies/mL viral load [111]. Tenorio and colleague mentioned that memory and naïve Treg cells numbers inversely correlates with HIV viremia [112]. In addition, the alteration of Th17/Treg balance may depend on multiple factors. Previous studies suggested that Th17 and Treg cells also have an important role in HIV disease progression. The role of Th17 in HIV-infected patients was first described in 2007; Meckanawat and colleague found that Th17 was higher in HIV-infected individuals when compared to uninfected individuals [113]. Furthermore, Ciccone and colleague found that in long term non-progressor (LTNP) HIV infection contained higher Th17 cells than in typical progressor patients [114]. However, the role of peripheral th17 cells in HIV infection is still unclear since the studies have demonstrated the differing results that Th17 cells are increased, decreased or unaltered when compared to uninfected subjects. While Th17 promoted proinflammatory function, Treg cells maintained self-tolerance and immune homeostasis. The role of

Treg in HIV -infected patients is still obscure. Some findings suggested that the suppressive function of Treg cells by reducing the chronic immune activation and inhibition of activated T cells can regulated the viral replication but on the other hand, suppression of HIV immune response can promote the viral persistence in the host [115, 116].